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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/785,276	02/16/2001	Robert Schlegel	MRI-007B	3373

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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/04/2002 10

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/785,276	SCHLEGEL ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *4,5,7-12,14-45,49-52 and 54-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,13,46-48 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed July 1, 2002. Currently, claims 1-66 are pending. Claims 4-5, 7-12, 14-45, 49-52, 54-66 have been withdrawn as drawn to non-elected subject matter.

Election/Restrictions

2. Applicant's election without traverse of Group I (Claims 1-3, 6, 13, 46-48, 53) in Paper No. 7 is acknowledged.

This application contains claims 4-5, 7-12, 14-45, 49-52, 54-66 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Sequence Rules

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.
For example, page 30, contains a sequence, however there is no sequence identifier.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-3, 6, 13, 46-48, 53 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility.

The claims are drawn to an isolated nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO: 32 or a complement thereof.

The specification teaches SEQ ID NO: 32 was identified by subtractive library hybridization techniques (page 94). The specification teaches that SEQ ID NO: 32 was identified from library cMhqaa. The specification teaches that the library-designated cMhqaa and cMhqsb was cDNA prepared from benign prostate hyperplasia and activated lymphocytes (page 94-95). The specification asserts that SEQ ID NO: 32 is a marker for prostate cancer.

In analyzing each of the tests for establishing utility, SEQ ID NO: 32 fails to have either a specific or substantial or a well-established utility.

First, the specification has not asserted a well established utility for SEQ ID NO: 32. Furthermore, the art does not teach any sequences which are related to SEQ ID NO: 32 and have a well-established utility.

Second, turning to substantial utility, the specification asserts that SEQ ID NO: 32 is a marker for marker for prostate cancer. A substantial utility is a utility that defines a “real world” use. Utilities that requires or constitute carrying out further research to identify or reasonably confirm a “real world” context of use are not substantial utilities. The asserted utility of a marker for prostate cancer is requires carrying out further research to reasonably confirm a “real world” use. The specification

assert that "as a greater number of patient samples are assessed for expression of the markers of the invention and the outcomes of the individual patients from whom the samples were obtained are correlated, it will also be confirmed that altered expression of certain of the markers of the invention are strongly correlated with malignant cancers and that altered expression of the markers of the invention are strongly correlated with benign tumors" (page 19, lines 26-32). This passage illustrates that as of the time of filing, the specification has not performed to analysis studies to determine whether SEQ ID NO: 32 has altered expression and whether the altered expression is strongly correlated with either malignant cancers of benign tumors. Therefore, the skilled artisan would be required to perform further research to confirm the use of SEQ ID NO: 32 expression as a marker for prostate cancer. The specification has not provided any indication of expression levels of SEQ ID NO: 32 in either normal tissue, benign tumors, or malignant prostate cancer. Therefore, determining whether the expression level of SEQ ID NO: 32 would first require the skilled artisan to ascertain the range of expression levels of SEQ ID NO: 32 within various tissues prior to being able to establish whether SEQ ID NO: 32 expression is indicative of normal, benign or malignant prostate tissues. Upon determining whether there is expression within these tissues, the skilled artisan would be required to determine the ranges of the expression to establish thresholds which would be indicative of normal, benign or malignant tissue state. Furthermore, the specification has provided no guidance as to whether SEQ ID NO: 32 is overexpressed in cancerous prostate tissue or whether SEQ ID NO: 32 is

underexpressed in cancerous prostate tissue. Each of these inquires are requires prior to the skilled artisan being able to use the claimed invention.

With respect to Claim 48, the specification does not provide any guidance to compounds for inhibiting prostate cancer. The skilled artisan would be required to provide further experimentation to confirm a real world use. Since the specification does not provide any compounds which inhibit prostate cancer, there is no guidance provided for compounds inhibiting prostate cancer.

As noted by Brenner v. Manson, 383 U.S. 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing...a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Therefore, since the specification fails to provide a well established or a substantial utility, the claimed invention lack utility.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-3, 6, 13, 46-48, 53 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to make and use the claimed invention.

The claims are broadly drawn to a nucleic acid comprising SEQ ID NO: 32. The claims further comprise kits with the intended use of assessing whether a patient is afflicted with prostate cancer or the presence of prostate cancer cells.

The art does not establish a correlation between SEQ ID NO: 32 and prostate cancer.

The specification teaches SEQ ID NO: 32 was identified by subtractive library hybridization techniques (page 94). The specification teaches that SEQ ID NO: 32 was identified from library cMhqaa. The specification teaches that the "driver" for library-designated cMhqaa and cMhqsb was cDNA prepared from benign prostate hyperplasia and activated lymphocytes (page 94-95). The specification teaches that the "tester" was cDNA generated from stage T3NO tumors (page 94, lines 22-24).

The teachings of the specification do not establish that one could actually detect expression of SEQ ID NO: 32 as an indicator of prostate cancer. The specification has performed a subtractive library hybridization technique in which the driver was prepared from benign prostate hyperpalsia and activated lymphocytes and wherein the tester was prepared from stage T3NO tumors. This difference detected by subtractive library hybridization technique does not establish that expression levels between benign prostate hyperplasia and tumors are significant in detecting prostate cancer. Rather the teachings of the specification assert that "as a greater number of patient samples are assessed for expression of the markers of the invention and the outcomes of the individual patients from whom the samples were obtained are correlated, it will also be confirmed that altered expression of certain of the markers of the invention are strongly

correlated with malignant cancers and that altered expression of the markers of the invention are strongly correlated with benign tumors" (page 19, lines 26-32). This passage illustrates that as of the time of filing, the specification has not performed to analysis studies to determine whether SEQ ID NO: 32 has altered expression and whether the altered expression is strongly correlated with either malignant cancers of benign tumors.

The specification has not provided any indication of expression levels of SEQ ID NO: 32 in either normal tissue, benign tumors, or malignant prostate cancer. Therefore, determining whether the expression level of SEQ ID NO: 32 would first require the skilled artisan to ascertain the range of expression levels of SEQ ID NO: 32 within various tissues prior to being able to establish whether SEQ ID NO: 32 expression is indicative of normal, benign or malignant prostate tissues. Upon determining whether there is expression within these tissues, the skilled artisan would be required to determine the ranges of the expression to establish thresholds which would be indicative of normal, benign or malignant tissue state. Furthermore, the specification has provided no guidance as to whether SEQ ID NO: 32 is overexpressed in cancerous prostate tissue or whether SEQ ID NO: 32 is underexpressed in cancerous prostate tissue. Each of these inquires are required prior to the skilled artisan being able to use the claimed invention.

While one could conduct additional experimentation to determine whether, e.g., expression of SEQ ID NO: 32 at certain levels might be associated with e.g., prostate cancer, the outcome of such research cannot be predicted due to the lack of guidance

from the specification and the art, and such further research and experimentation are both unpredictable and undue. It is further unpredictable as to whether any quantity of experimentation would allow one to practice the claimed invention. Accordingly, it would require undue experimentation for a skilled artisan to use the claimed invention.

Moreover, the specification has not taught how to make the invention as broadly as claimed. The specification teaches a single nucleic acid sequence within this large genus, namely a nucleotide sequence consisting of SEQ ID NO: 32, 396 nucleotides in length. The specification, while teaching that larger sequences may be obtained (page 29, lines 4-10), the specification fails to provide a description of these larger sequences, namely full open reading frames, genes, homologoues, variants. In the instant case, Applicant has defined only a fragment of a nucleic acid sequence, namely SEQ ID NO: 32. Applicant has not disclosed any genomic DNA sequences and particularly has not disclosed any intron sequences or regulatory sequences. Moreover, the claims encompass sequences from closely related sequences which are either splice variants, homologues from other organisms, or variants minimally comprising SEQ ID NO: 32. The claims which allow for nucleic acids which hybridize selectively to SEQ ID NO: 32 also have not been described, for the reasons provided above. Hybridization language allows for variations in sequences which have not been described. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus such that the skilled artisan could make the invention as broadly as claimed.

With respect to Claim 48, the specification does not provide any guidance to compounds for inhibiting prostate cancer. The skilled artisan would be required to provide further undue experimentation to determine which compounds inhibit prostate cancer. There is no compound provided in the specification which inhibits prostate cancer and there is no guidance provided for compounds inhibiting prostate cancer. Therefore, absent further experimentation, the skilled artisan would be unable to provide compounds which inhibit prostate cancer in patients.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 6, 13, 46-48, 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to an isolated nucleic acid molecule comprising a nucleotide sequence of SEQ ID NO: 32, or a complement thereof (Claim 1). The claims further claim a compound which selectively hybridizes to a nucleic acid molecule comprising SEQ ID NO: 32.

The claims broadly encompass full cDNA molecules, genes including introns, exons and regulatory regions, alleleic variants comprising SEQ ID NO: 32, splice

variants comprising SEQ ID NO: 32, homologues comprising SEQ ID NO: 32, and numerous other sequences.

The specification teaches a single nucleic acid sequence within this large genus, namely a nucleotide sequence consisting of SEQ ID NO: 32, 396 nucleotides in length. The specification, while teaching that larger sequences may be obtained (page 29, lines 4-10), fails to provide a description of these larger sequences, namely full open reading frames, genes, homologoues, variants. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA…' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus

claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, Applicant has defined only a fragment of a nucleic acid sequence, namely SEQ ID NO: 32, this structure does not constitute a substantial portion of the claimed genus of genes, variants, homologs, etc. Applicant has not disclosed any genomic DNA sequences and particularly has not disclosed any intron sequences or regulatory sequences. Moreover, the claims encompass sequences from closely related sequences which are either splice variants, homologues from other organisms, or variants minimally comprising SEQ ID NO: 32. The claims which allow for nucleic acids which hybridize selectively to SEQ ID NO: 32 also have not been described, for the reasons provided above. Hybridization language allows for variations in sequences which have not been described. Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

With respect to Claim 48, the specification does not described any compounds for inhibiting prostate cancer. Since no compound has been provided in the specification which inhibits prostate cancer, there is no guidance provided for compounds inhibiting prostate cancer. The specification fails to describe any member of the claimed genus of compounds for inhibiting prostate cancer. Therefore, the specification does not describe compounds for inhibiting prostate cancer.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Perkin Elmer Catalog ("PCR Systems, Reagents and Consumables", 1995-1996, page 52-53).

It is noted that the intended us of the kit, i.e. for assessing whether a patient is afflicted with prostate cancer, does not carry patentable weight. Therefore, the kit merely contains reagents for assessing expression of a SEQ ID NO: 2. This kit reads on a simple sequencing kit.

The Perkin Elmer Catalog teaches PCR application kits DNA sequencing. Specifically the Amplicycle Sequencing kit contains DNA polymerase, G, A, T and C termination mix, primers, stop solution. Each of these components would allow for determining expression of SEQ ID NO: 32. Therefore, Perkin Elmer teaches every limitation of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 46-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan (US Pat. 5,474,796, December 1995) in view of Ahern (The Scientist, Vol 9, No. 15, page 20, July 1995).

Brennan teaches an array of oligonucleotides having 10 nucleotides each (10-mer). Brennan teaches that every possible permutation of the 10-mer oligonucleotide are provided on the solid support.

Brennan does not specifically teaches packaging necessary reagents into a kit.

However, Ahern teaches reagent kits offer scientists good return on investment. Ahern teaches kits save time and money because the kits already comes prepared.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Brennan with the teachings of Ahern to incorporate the necessary reagents into a packaged kit. The ordinary artisan would have been motivated to have packaged the primers, probes, and reagents of Brennan into a kit, as taught by Ahern for the express purpose of saving time and money.

Conclusion

9. No claims allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
October 28, 2002

W. Gary Jones
Supervisory Patent Examiner
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